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Telehealth for patients at high risk of cardiovascular disease: pragmatic randomised controlled trial

Chris Salisbury, Alicia O'Cathain, Clare Thomas, Louisa Edwards, Daisy Gaunt, Padraig Dixon, Sandra Hollinghurst, Jon Nicholl, Shirley Large, Lucy Yardley, Tom Fahey, Alexis Foster, Katy Garner, Kimberley Horspool, Mei-See Man, Anne Rogers, Catherine Pope, Alan A. Montgomery

Centre for Academic Primary Care, School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol BS8 2PS

Chris Salisbury
Professor of Primary Health Care
Clare Thomas
Programme Manager
Louisa Edwards
Trial manager
Padraig Dixon
Senior Research Associate in Health Economics
Sandra Hollinghurst
Senior Lecturer in Health Economics
Katy Garner
Research Associate
Mei-See Man
Trial Manager

School of Health and Related Research (ScHARR), University of Sheffield, 30 Regent Street, Sheffield, S1 4DA

Alicia O'Cathain
Professor of Health Services Research
Jon Nicholl
Dean of School
Alexis Foster
Study Manager
Kimberley Horspool
Study Manager/Research Associate

Bristol Randomised Trials Collaboration, School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS

Daisy Gaunt
Research Associate in Medical Statistics

NHS England South (Wessex), Room F18, First Floor, Oakley Road, Southampton, SO16 4GX

Shirley Large
Screening and Immunisation Co-ordinator

Department of Psychology, University of Southampton, University Road, Southampton, SO17 1BJ

Lucy Yardley

Professor of Health Psychology

RCSI, Department of General Practice, Beaux Lane House, Lower Mercer Street, Dublin 2

Tom Fahey

Professor of General Practice

Faculty of Health Sciences, University of Southampton, 104 Burgess Rd, Southampton SO17 1BJ

Anne Rogers

Professor of Health Systems Implementation

Catherine Pope

Professor of Medical Sociology

Nottingham Clinical Trials Unit, Nottingham Health Science Partners, C Floor, South Block, Queen's Medical Centre, Nottingham, NG7 2UH

Alan A Montgomery

Professor of Medical Statistics and Clinical Trials

Correspondence to:

Prof Chris Salisbury

c.salisbury@bristol.ac.uk

What this paper adds

What is already known

- Given the rising prevalence of long term health conditions, it is necessary to explore new ways to deliver health care and to support self-management in order to expand provision of care at low cost.
- There is considerable optimism amongst policy-makers that greater use of digital health technologies ('telehealth') in combination with new ways of working could transform health care delivery, helping the NHS to be sustainable.
- Evidence about the effectiveness of telehealth interventions is equivocal, with some benefits from specific technologies but little evidence of effectiveness in 'real world' implementation.

What this study adds

- This pragmatic trial assessed the effectiveness and cost-effectiveness of an intervention for people with high risk of cardiovascular disease which combined the use of a range of digital health technologies with telephone support from trained lay health advisors.
- We found some evidence that the intervention led to modest improvement in overall cardiovascular risk for a minority of participants, but had no impact on average risk, although it was associated with improvements in specific risk factors and patient perceptions of support and access to care.

Abstract (online version)

OBJECTIVES

To assess whether non-clinical staff can effectively manage people at high risk of cardiovascular disease using digital health technologies.

DESIGN

Pragmatic, multi-centre, randomised controlled trial.

SETTING

Participants recruited from 42 general practices in three areas of England

PARTICIPANTS

Between 3 December 2012 and 23 July 2013 we recruited 641 adults aged 40 to 74 years with 10 year cardiovascular disease risk ≥20%, no previous cardiovascular event, at least one modifiable risk factor (systolic BP ≥140; body mass index ≥30; current smoker) and access to telephone, internet and email.

INTERVENTIONS

Participants individually allocated to intervention (n= 325) or control (n= 316) using automated randomisation stratified by site, minimised by practice and baseline risk score. Intervention: The Healthlines Service (alongside usual care), comprising regular telephone calls from trained lay health advisors following scripts generated by interactive software. Advisors facilitated self-management by supporting participants to use online resources to reduce risk factors and sought to optimise medication, improve treatment adherence and encourage healthier lifestyles. Control: usual care alone.

MAIN OUTCOME MEASURES

Primary outcome: proportion of participants responding to treatment, defined as maintaining or reducing their cardiovascular risk after 12 months. Outcomes were collected 6 and 12 months after randomisation and analysed masked. Participants were not masked.

RESULTS

50.2% (148/295) of intervention group participants responded to treatment compared with 42.6% (124/291) in the control group (adjusted odds ratio 1.3; 95% confidence interval 1.0 to 1.9; number needed to treat = 13); a difference possibly due to chance (p=0.079). The intervention was associated with reductions in BP (difference in mean systolic -2.7 mmHg (-4.7 to -0.6), mean diastolic -2.8 (-4.0 to -1.6)); weight (-1.0 kg (-1.8 to -0.3)), and body mass index (-0.4 (-0.6 to -0.1)) but not cholesterol (-0.1 (-0.2 to 0.0), smoking status (adjusted OR 0.4 (0.2 to 1.0)), or overall cardiovascular risk as a continuous measure (-0.4 (-1.2 to 0.3)). The intervention was associated with improvements in diet, physical activity, medication adherence, and satisfaction with access to care, treatment

received and care co-ordination. There was one serious related adverse event: a participant hospitalised with low BP.

CONCLUSIONS

This evidence based telehealth approach was associated with small clinical benefits for a minority of people with high cardiovascular risk, and there was no overall improvement in average risk. However, the Healthlines Service was associated with improvements in some risk behaviours, and in perceptions of support and access to care.

TRIAL REGISTRATION

Current Controlled Trials (ISRCTN 27508731).

(403 words)

Introduction

The growing prevalence of long-term conditions means that new and more efficient approaches to health care delivery are needed which support people to manage their own care, with less reliance on consultations with expensively trained health care professionals. Effective self-management, as part of a shift in the management of long-term conditions, can help improve health outcomes and reduce costs.[1 2] Many countries are exploring a greater use of technologies such as the internet, remote monitoring, and telephone support as a way of expanding provision and increasing access to care for a large number of people at relatively low cost. In the UK, current policy envisages these 'telehealth' approaches as having potential to transform the delivery of health care in order to make the NHS sustainable for the future.[3] In the United States, the Veterans Health Administration has enrolled more than 50,000 people in a home telehealth program, [4 5] and in Europe the Renewing Health Consortium is evaluating telehealth programmes in nine countries.[6]

There is a burgeoning volume of literature on the effectiveness of specific telehealth interventions, with promising effects for some applications. However, recent reviews have highlighted that much of the evidence is of poor quality, results are inconsistent, there is a lack of theoretical underpinning which makes it difficult to interpret the mixed results, and there is some evidence of publication bias

in favour of positive results.[7-10] Furthermore, focusing on specific applications or technologies in isolation is of limited value since they need to be considered in the context of their implementation within the health care system. In practice, large scale health care programmes based on telehealth involve the combined use of technologies, for example online programs and/or remote monitoring with telephone support from advisors following computerised algorithms. In the recent 5 year strategic plan for the NHS, it is argued that evaluation is needed of 'combinatorial innovation', in which a range to technologies are provided in combination with new ways of working.[11 12] There are very few rigorous pragmatic studies of real world implementation of this approach.[8] Furthermore, a key aspect of the argument for telehealth is increased efficiency, but there are few studies incorporating economic analyses and the limited evidence available suggests that many telehealth interventions are not cost-effective.[13]

We conducted a research programme to develop a conceptual model for the effective use of telehealth in long-term conditions, based on literature reviews,[14 15] qualitative research[16] and surveys of patient views.[17] Designated the Telehealth in Chronic Disease (TECH) model, this builds on existing approaches such as the Chronic Care Model by creating a framework for improving chronic disease management via telehealth.[18] We used this model to design the Healthlines Service for the management of long-term conditions, based on the combined use of internet based health applications which had evidence of effectiveness supported by non-clinically qualified staff working using tailored computerised algorithms.[19]

We evaluated the Healthlines Service through linked pragmatic multi-centre randomised controlled trials with nested process and economic evaluations in two exemplar conditions: depression or raised cardiovascular risk. This paper reports the findings with regard to patients with raised cardiovascular risk. Although hypertension, obesity and hyperlipidaemia are often considered as long-term conditions, it is more appropriate to consider them as risk factors, with their combined effect determining overall cardiovascular risk.[20] This was considered an appropriate exemplar because of the very high number of people affected (10% of adults aged 35-74 in England and Wales have 10 year cardiovascular risk ≥20%),[21] which has serious health consequences due to heart attacks, strokes, kidney disease and other problems. Cardiovascular disease causes 28% of deaths in England, accounts for 10% of all hospital admissions, and involves an annual expenditure in England of almost £7 billion.[22] A low cost intervention which could be made widely available to large numbers of individuals could have a beneficial impact at a population level even if the effect for an individual was small.

There is existing evidence for the effectiveness of specific relevant technological approaches, such as home BP monitoring,[23] mobile phone applications to support smoking cessation,[24] and online

interventions for weight loss.[25] This provided a good basis for the hypothesis that combining these 'active ingredients' and implementing them within a new telehealth model of care would be effective and cost-effective. Furthermore, the introduction in 2008 of the NHS 'Health Check' programme was likely to identify a large number of people with high cardiovascular risk, and there was a need to explore ways to expand provision of care to manage them once they had been identified.[26]

Our hypothesis was that the Healthlines Service for patients with high cardiovascular risk would be more clinically and cost-effective than usual care, while also improving participant's quality of life, risk behaviours, and experience of care.

Methods

Design

This was a pragmatic, multi-centre, randomised controlled trial comparing the Healthlines Service in addition to usual care versus usual care alone in adults with a high risk of cardiovascular disease. The study was registered prior to recruitment of the first participant and the study protocol has been published.[19] There were no important changes to the methods after the trial commenced, apart from the addition of a nested sub-study of different forms of patient invitation information to assess the impact on participant recruitment rates. This did not alter the design or outcomes for the main trial; results of this sub-study are published elsewhere. [27]

Participants

Patients eligible for the trial were aged between 40 and 74 years of age, had a risk of a cardiovascular event in the next 10 years of ≥20% calculated using the QRISK2 score,[21] and had one or more of the following modifiable risk factors (systolic blood pressure (BP) ≥140, body mass index (BMI) ≥30, and/or being a current smoker). Participants required access to a telephone, the internet, and an email address. We excluded people who had a previous cardiovascular event; were pregnant or planning pregnancy; had a serious mental health problem, dementia, severe learning disability, or substance dependency; were receiving palliative care; or were unable to communicate verbally in English.

Participants were recruited from 42 general practices covering populations with a range of socio-demographic characteristics in and around Bristol, Sheffield and Southampton, England. We used patients' medical records to identify individuals who had at least one modifiable risk factor and estimated 10 year cardiovascular risk of ≥18% (we were over-inclusive at the initial screening stage because QRISK2 scores based on historical records may not reflect current risk and we wanted to invite potentially eligible individuals to have an updated risk assessment). A random sample of these

potentially eligible patients in each practice was sent postal information about the study, after GPs screened the list for patients with known exclusion criteria. We sent information to between 250 and 285 patients in each practice, altering the sampling fraction over time in order to achieve our recruitment targets. Patients who expressed an interest in the study were telephoned by a researcher to conduct initial eligibility screening and then invited for an assessment of cardiovascular risk status by a practice nurse at their participating general practice. The nurse measured the patients' BP, weight and height, smoking status and total cholesterol to high-density lipoprotein ratio, and collected all other relevant information needed to calculate the patient's QRISK2 score (see Appendix 1). Patients who had a QRISK2 score ≥20% and had one or more of the specified modifiable risk factors completed a baseline questionnaire and consent form, either online or by post.

Intervention and control

Participants in the control group could continue to receive all care normally provided by the NHS, but they did not have any contact with the Healthlines Service. Usual care involved management of cardiovascular risk factors by primary care clinicians, including in some cases referral to community services for advice about smoking cessation and weight management.

Participants in the intervention arm received support from the Healthlines Service in addition to usual NHS care as described above. The Healthlines Service is a multi-faceted intervention, incorporating a range of strategies to address the various components of the TECH model,[18] as shown in Box 1. The intervention is based around regular telephone calls from a health advisor, supported by patient-specific tailored algorithms and standardised scripts generated through a computerised behavioural management programme. This programme was originally developed and successfully evaluated in the USA by Bosworth et al and includes a series of modules on subjects such as medication adherence, diet and smoking cessation.[28 29] The standardised scripts generated by the software were based on recognised behaviour change principles, such as stimulus control, problem solving, cognitive restructuring, and goal setting.[30] We modified the programme to reflect English management guidelines and referral options, wrote additional modules with new content and adapted the language to suit an English population.

Health advisors telephoned each participant for an initial assessment of their health needs and to agree their specific goals. Following the initial call, the advisors telephoned each participant approximately every month for one year. The software was interactive and provided different computerised scripts so that the content of each call was tailored to meet each participant's individual needs and goals. The software provided health advisors with links to relevant and quality assured online resources and applications to support self-management (for example, to help with

losing weight or stopping smoking) and the advisors sent these links to participants by email or by post. Each participant was telephoned by the same advisor on each occasion when possible in order to avoid an anonymous 'call-centre' approach, since our earlier qualitative research had identified a relationship with the advisor as an important factor in engaging prospective participants.[15] The Healthlines Service was designed to improve access to care and was available until 8pm on weekdays and 2pm on Saturdays.

Participants were also provided with access to a Healthlines web portal where they could obtain further information about cardiovascular disease, access other online resources, request a call-back from Healthlines staff, see copies of letters to their GP and use a BP self-monitoring system. Participants with a baseline systolic BP ≥ 140 were offered an Omron M3 validated home BP monitor by their practice nurse, requested to take their BP twice daily for the first week and weekly thereafter, and to upload their readings to the Healthlines portal. The portal calculated average readings over the previous six days initially and then over the previous six weeks thereafter. Using these readings, the participant was automatically advised by the portal whether their BP was within their target, when to take their BP again and what to do if their BP was too high or too low. Target BP was based on UK guidelines,[31] although an individual's target could be modified by their GP. Average BP readings were reviewed by health advisors at each telephone call, and participants with above target readings were asked to see their GP to review their treatment. Advisors sent an email to the GP, attaching details of the patient's recent BP readings and a summary of NICE guidelines about recommended steps for intensifying treatment.

The Healthlines advisors were not clinically qualified but had experience working as health advisors for NHS Direct and had a further three weeks of training in health coaching, motivational interviewing, treatment options (including medication) for hypertension, smoking and obesity, and use of the Healthlines computerised management programme.

The Healthlines Service was originally hosted by NHS Direct, which provided a range of telehealth services through a network of call centres and a nationally recognised website. When NHS Direct closed in March 2014 delivery of the intervention was paused for two months while the staff and computer systems were transferred to a new provider (Solent NHS Trust). Although the Healthlines Service resumed unaltered after this hiatus, about two-thirds of participants experienced some disruption and some participants could not receive the full number of telephone calls during their 12 month follow-up period.

Outcomes

The primary outcome was the proportion of participants responding positively to treatment, defined as maintaining or reducing their 10 year cardiovascular risk 12 months after randomisation,

estimated using the QRISK2 score. Since cardiovascular risk increases with age, maintaining or reducing risk over 12 months requires an improvement in at least one modifiable risk factor. We treated QRISK2 score (continuous) as a secondary outcome. The estimate of risk was based on data collected at an assessment by a nurse or health care assistant at the participant's general practice at 6 and 12 months after recruitment using the same procedures as used at baseline (see Appendix 1). Follow-up QRISK2 scores were calculated by updating age and values for modifiable risk factors only. Other variables such as diagnoses of atrial fibrillation or diabetes were not altered to avoid bias due to the greater attention paid to participants in the intervention arm.

Cardiovascular risk is a composite outcome, and the individual risk factors of BP, weight (and body mass index), smoking and cholesterol were important secondary outcomes. Other secondary outcomes were quality of life; exercise; diet; satisfaction with treatment received and with amount of support received; perceived access to care; self-management skills and self-efficacy; medication adherence; health literacy; use of telehealth and perceptions of care co-ordination. The specific measurement instruments used are referenced in Table 6. Secondary outcome measures were collected through patient questionnaires, completed online or by post, at baseline and 6 and 12 months after randomisation. Data about prescriptions and primary care consultations were obtained from general practice records while details of use of the intervention were obtained from Healthlines Service records. Potential serious adverse events were identified through reports from participants or health professionals, further enquiry about hospital admissions reported in outcome questionnaires, or admissions, deaths or other potential serious adverse events identified through review of primary care notes at the end of the trial. All such events were logged with a description of the event and an assessment of expectedness, relatedness and seriousness and reported to the trial monitoring committee, sponsor and ethics committee as appropriate.

Sample size

The sample size was chosen pragmatically, taking into account the size of effect that would be likely to influence practice and which might be feasible to detect in a trial of reasonable size. Based on a previous study we assumed that 35% of participants in the control arm would maintain or reduce their cardiovascular risk over 12 months.[38] Including 240 participants per trial arm for analysis would provide 80% power (5% alpha) and 90% power (1% alpha) to detect differences of 13 and 18 percentage points, respectively. Assuming 20% attrition, we therefore aimed to recruit 600 participants, 300 in each trial arm.

Randomisation and masking

Participants providing consent were individually randomly allocated in 1:1 ratio to the intervention or usual care group. Allocation was made using a web randomisation system hosted by the Bristol

Randomised Controlled Trials Collaboration, and automated to ensure concealment. Randomisation was stratified by location of recruitment (Bristol, Sheffield, or Southampton) and minimised by general practice and baseline QRISK2 score. Participants were notified of their allocation by the researchers by email. Participants were not masked to treatment allocation. Data for the QRISK2 score were collected by practice nurses or health care assistants, who may have been aware of treatment allocation at follow-up, but the variables of relevance on smoking (validated using a carbon monoxide monitor), BP and cholesterol were all based on objective quantitative data. All other outcome data were collected by participant self-report or electronic download from medical records and were entered and analysed blinded to treatment allocation.

Statistical analysis

Analysis was conducted according to CONSORT guidelines, following an analysis plan agreed in advance with the independent Trial Steering Committee and Data Monitoring Committee. Descriptive statistics were used to compare baseline characteristics of trial participants by allocated arm. The primary analysis of response to treatment after 12 months was conducted using a mixed effects logistic regression model adjusted for site, baseline QRISK2 score, and general practice (as a random effect). Participants were analysed according to allocated arm. We conducted sensitivity analyses of the primary outcome using: the assumption that all participants were exactly one year older at 12 months follow-up; simple imputation of missing outcome data that assumed no treatment response; multiple imputation of missing data; exclusion of GP practice as a random effect; and adjustment by time between randomisation and follow-up. By fitting interaction terms between trial arm and subgroup variables, we investigated whether any effect of the Healthlines intervention on the primary outcome differed according to subgroups defined by sex, age, baseline QRISK2 score, and presence or absence of each of the modifiable risk factors (hypertension, obesity, smoking) at baseline.

In secondary analysis of the primary outcome, we estimated the complier-average causal effect (CACE) of the Healthlines intervention when received as intended. We described compliance as little or none (two or fewer telephone calls), partial (three to 11 calls) or full (12 or 13 calls). We estimated the CACE at 12 months using principal stratification in two ways, classifying partial compliers as either non-compliers or full compliers respectively.[39]

Secondary outcomes were analysed in a similar manner to the primary outcome. Between-group effects were estimated using linear, logistic or binomial mixed effects regression models, adjusted for stratification and minimisation variables and value of the outcome at baseline. Participants were analysed as randomised without imputation of missing data. In order to reduce the number of statistical comparisons, we estimated between-group differences for secondary outcomes (other

than cardiovascular risk factors) only at the final 12 month follow-up time-point. We described serious adverse events by study arm.

We assessed the cost-effectiveness of the Healthlines intervention from an NHS perspective at 12 months from randomisation. Cost-effectiveness was not listed as a secondary outcome in the trial registry because we viewed it as an approach to analysis rather than as an outcome; however assessment of cost-effectiveness was specified *a priori* as an aim in the registry and described in the published protocol. The methods and results of the economic evaluation will be described in detail elsewhere. In brief, health system costs were compared with incremental quality-adjusted life years (QALYs), measured using the EQ-5D-5L generic quality of life questionnaire[32] at baseline and six and 12 months post-randomisation, in order to produce an estimate of net monetary benefit. We also developed a cohort simulation model in order to estimate the cost-effectiveness of the intervention over the estimated remaining lifetime of trial participants.

All analyses were conducted using Stata version 13 MP2. The trial was registered prospectively with Current Controlled Trials (ISRCTN 27508731).

Patient involvement

There was strong and valuable patient and public involvement throughout the Healthlines research programme. Two service user groups (Mental Health Research Network and NHS Direct user group) provided feedback on the initial questionnaire about patients' preferences and needs in relation to telehealth which helped to inform the intervention design.[17] Two representatives of these groups became members of the Management Group for the five year research programme. They contributed to the design of the patient survey,[17] participated in a workshop to develop the TECH model which underlies the intervention,[18] and became members of the Trial Steering Committee for the randomised trial.[19] They commented on the acceptability of the intervention to potential participants and obtained feedback from their user groups on the outcome measures. At the end of the trial they contributed to a workshop of key stakeholders that was held to discuss interpretation and dissemination of the findings. They also provided useful feedback on the final report of the programme, and in particular the lay summary. We have thanked all participants for their involvement and given them details of the website where all published results will be made publically available (http://www.bristol.ac.uk/healthlines/).

Results

Participants were recruited between 3 December 2012 and 23 July 2013. Of 7,582 people sent information about the study, 1205 (16%) individuals expressed interest and were assessed. Of these, 641 were eligible and randomly allocated to the Healthlines intervention (n=325) or usual care arms

(n=316) (Figure 1). 597 (93%) of participants provided follow-up data after 6 months follow-up and 586 (91%) after 12 months follow-up (the primary outcome).

Characteristics of participants in the trial are shown in Table 1. Overall, the participants were at high risk of a cardiovascular event (mean 10 year risk 31%) due to combinations of modifiable and non-modifiable risk factors. Participants were predominantly white men aged over 60, and at baseline 356 (56%) had obesity (BMI>=30), 450 (70%) had a BP≥140 and 528 (18%) were currently smoking. The two trial arms were well balanced except that there were fewer smokers and more participants with diabetes in the intervention arm. These factors both contribute to the baseline QRISK2 score, which was included as a covariate in all analyses, so we did not conduct additional statistical adjustment for these imbalances.

Primary outcome

After 12 months, a slightly higher proportion of participants in the intervention arm had improved or maintained their cardiovascular risk compared with the usual care arm (50.2% versus 42.6% respectively; number to treat 13), although this apparent difference had wide confidence intervals and could be due to chance (adjusted odds ratio 1.3 [95% confidence interval 1.0 to 1.9]; p=0.079). This conclusion was largely unchanged in our sensitivity analyses (Table 2). There was no evidence that the intervention was differentially effective for any of the pre-specified sub-groups defined by baseline characteristics, although the study was not powered to detect these interaction effects (Table 3).

Secondary outcomes

There was no evidence of any between group difference in the proportion of participants who improved or maintained their cardiovascular risk after 6 months follow-up (Table 2). There was also no evidence of difference between groups in QRISK2 score when treated as a continuous measure (Table 4). However, the intervention was associated with improvements in some of the individual modifiable risk factors which contribute to cardiovascular risk, including reductions in systolic and diastolic BP and in weight and body mass index after 12 months follow up (Table 4). The intervention did not lead to improvements in cholesterol levels (Table 4) or rates of smoking (Table 5).

Table 6 shows that the intervention was associated with improvements in several of the secondary outcomes. Participants in the intervention arm reported that they improved their diets and increased their level of exercise. They were more likely to adhere to their treatment with statins and with anti-hypertensive medication. Intervention arm participants reported improved access to care, and expressed greater satisfaction with the amount of support they received and their overall treatment. They also reported that their care was better organised and co-ordinated. For ease of

presentation, Table 6 only shows data on secondary outcomes after 12 months follow-up. Findings after six months are available from the authors.

After 12 months, the incremental cost-effectiveness ratio was estimated to be £10,859 in 2012/13 prices (incremental cost £138 [£66 to £211]; incremental QALY gain 0.012 [-0.001 to 0.026]). The net monetary benefit at a cost-effectiveness threshold of £20,000 was estimated to be £116 (95% CI: -£58 to £291). The intervention was likely to be cost-effective at this threshold after 12 months with a probability of 0.77. The cohort simulation study showed that the lifetime cost-effectiveness of the intervention increased the greater the duration of effect of the intervention on cardiovascular disease risk beyond the follow-up period of the trial. Further details will be published elsewhere.

Engagement with the intervention

Participants in the intervention arm received a median of 10 (IQR 8 to 12) encounters with the Healthlines cardiovascular service out of a possible maximum of 13 encounters. The mean duration of each encounter was 18 (SD 9.5) minutes. Using a complier-average causal effect (CACE) analysis we explored whether the number of encounters received in the intervention arm was associated with the primary outcome. The results suggest an increase in effect of the intervention amongst participants who received all or most of the planned number of encounters (Table 7).

Participants in the intervention arm logged in to the Healthlines website on a median of 14 (IQR 3 to 47) occasions, more than once a month. 296 (91%) of participants were given a BP monitor, of which 200 entered at least one reading, uploading a median of 70 (IQR 48 to 102) BP readings.

Healthlines advisors sent a median of 5 (IQR 2 to 9) letters by email to participants' GPs. Of these, 138/310 of the participants' GPs were sent letters advising commencement or review of BP medication, 32 (10%) were asked to consider starting statin therapy, 7 (2%) were asked to prescribe orlistat for obesity and 3 (1%) were asked to prescribe medication to aid smoking cessation.

However, based on data from the medical records, there were no differences between the intervention and control group in the number of changes in medication (starting new treatments or changing dose) for hypertension or lipid-lowering drugs, with a median of zero (IQR 0 to 1) changes for both types of treatment. Similarly, there was no evidence of difference between the arms in the proportion of participants who reported taking statins or medication for hypertension, the proportion who had a change in treatment prescribed, or the types of medication prescribed (Table 8). These data were not specified as outcomes but are presented here to explore the mechanism of effect of the intervention.

Over the 12 month period, there was no evidence of difference between the intervention and control arms in the number of times participants consulted in primary care (mean 11.28 (SD 8.8, n=313) and 11.42 (SD = 7.9 n=325) respectively, adjusted incidence ratio 0.99 (0.89 to 1.09, p=0.77)).

Patient safety

Over the course of the trial there were 76 adverse events reported by participants, 38 in each trial arm. There were 24 serious and unexpected events in the usual care arm and 22 in the intervention arm (Appendix 2). Only one serious event in the intervention arm was likely to be related: a participant was hospitalised with low BP which could have been due to not reducing his antihypertensive medication after he had lost weight.

Discussion

Principal findings

This study suggests a modest benefit from the Healthlines Service in terms of the proportion of individuals reducing or maintaining their cardiovascular disease risk over 12 months. Despite the large sample size, the estimate of effect has wide confidence intervals and could be consistent with no effect or a 90% increase in the odds of reducing/maintaining risk. The results for the primary outcome were not statistically significant in either the complete case analysis or after multiple imputation of missing data. Furthermore, there was no evidence of difference between the trial arms in average risk, treating QRISK2 as a continuous measure (a secondary outcome).

Cardiovascular risk is a composite measure, based on several underlying risk factors. The Healthlines intervention was associated with small but meaningful improvements in several of these factors, including reductions in BP and weight, but not in cholesterol or smoking. It was also associated with improvements in self-management behaviours such as diet and physical activity, better adherence to medication, and greater participant satisfaction with support, access to care and treatment received. It is important to note that these improvements in self-management behaviours would reduce cardiovascular risk beyond the benefit captured in the QRISK2 score and are also likely to reduce risk for many other common and serious diseases, so our focus on cardiovascular risk measured using QRISK2 is likely to be conservative in terms of estimating overall benefit.

The intervention was not successful at promoting optimisation of drug treatment in line with current guidelines, which was a key intended mechanism for reducing BP and cholesterol levels. This is consistent with previous research highlighting the problem of clinical inertia – that treatment is not necessarily intensified in people who fail to reach treatment targets even when regular monitoring shows inadequate control.[40] Although the observed reduction in cardiovascular risk was small (and could be due to chance), the likely reduction in cardiovascular events in the longer term means that the Healthlines Service was likely to be cost-effective.

Strengths and limitations

This appears to be the largest pragmatic trial so far conducted of a telehealth intervention to reduce cardiovascular risk. It is a complex intervention combining a range of telehealth approaches, and has a strong theoretical foundation based on the underlying TECH conceptual model.[18] The large sample size and high level of participant retention enhance internal validity, while the multi-centre recruitment and broad inclusion criteria enhance external validity.

The Healthlines intervention incorporates the use of a number of telehealth approaches which have reasonable evidence of effectiveness, such as home BP monitoring, and we sought to implement them on a wide scale. Most research studies of telehealth interventions relate to specific technological innovations and can be characterised as efficacy trials, in that they demonstrate the effect of a well-defined intervention in individuals with tightly defined inclusion and exclusion criteria, and who are motivated to use the particular application. These studies may lead to estimates of effect which are exaggerated when compared with the effects observed when the application is implemented more widely. By contrast this trial was pragmatic, testing an intervention as delivered by a mainstream NHS provider in a way that could be rolled out quickly on a wide scale.

There are several limitations. Firstly, only 16% of those sent information about the study expressed interest in it. This response rate is not unusual in primary care based trials in which people who may not have an expressed health need are invited to take part in research, indeed the response rate in this trial was higher than in several other influential trials of related interventions.[41-43] However, if non-respondents differ from respondents because of disinterest in research this could reduce the generalisability of trial findings. Based on information from 2741 people who gave a reason for non-participation the most common reasons were related to technology rather than research: 1491 (54%) had no internet access and 1225 (45%) did not feel confident using computers (people could provide more than one reason).[44] Many people 1135 (41%) did not feel they needed additional support with health issues. It is important to note that less than half of those invited for an NHS Health Check attend, and not everyone who smokes or is over-weight is motivated to change. We also recognise that telehealth interventions are not necessarily of interest to everyone and take-up in routine service use may be low. However, health care is likely to be increasingly personalised, with different forms of care being chosen by different groups in the population. Telehealth interventions may be useful for a minority of potential participants if (as in the case of raised cardiovascular risk) the total number of people at risk is large.

Second, the closure of NHS Direct towards the end of the trial meant that delivery of the intervention was disrupted and many participants received less than the full course of intervention encounters. However the fact that we were able to move the service quickly to another provider

demonstrates the transferability of the approach. Third, we analysed a large number of secondary outcomes in order to capture the range of potential effects from this complex intervention, but this raises the possibility of some apparent differences being due to chance because of multiple testing. Fourth, the sample size was chosen pragmatically and assumed that 35% of control arm participants would maintain or reduce the cardiovascular risk over 12 months. In the trial, a higher than anticipated proportion of those in the control group achieved this, perhaps because of the impact of the NHS Health Checks programme.[26] This reduced the power of the study to detect differences between the intervention and control groups, but this will have been mitigated to some extent by the fact that we recruited and successfully followed up more patients than anticipated. Fifth, the study was limited to patients under 75 years of age (because this is the age range in which QRISK2 has been validated and is also the age-group targeted by NHS Health Checks), but this intervention could potentially also help older people. The study also excluded people without access to the internet, however the proportion of the population with access is increasing rapidly.

Finally, the use of cardiovascular risk as a composite outcome has limitations because the QRISK2 score is strongly dominated by non-modifiable factors such as age and sex. We chose to analyse the QRISK2 as a binary measure of 'response to treatment' for the primary outcome because this approach is sensitive to changes in modifiable risk factors. The number of patients 'needed to treat' to gain benefit from the intervention was 13. However, because only a minority of participants benefited, there was no significant change in QRISK2 averaged across all participants when analysed as a continuous variable (a secondary outcome). Nevertheless the small changes in modifiable risk factors observed in this trial are likely to be associated with meaningful benefits. Based on the systematic review by Law et al,[45] the reductions in blood pressure observed in this trial would lead to a 23% reduction in the relative risk of stroke and a 15% reduction in the relative risk of a heart attack. The combined effect (along with the reduction in weight) suggests that these small changes in modifiable risk factors are likely to be worthwhile, particularly at a population level when applied to the very large number of people with high risk of cardiovascular disease.

Comparison with other studies

This was a trial of the implementation of the combined use of a range of telehealth interventions to address cardiovascular risk factors. The results are broadly consistent with earlier trials which have studied different components of the intervention in isolation to reduce individual risk factors. A systematic review of trials of BP self-monitoring showed that this was associated with small reductions in both systolic and diastolic BP of a similar size to those achieved in the Healthlines CVD risk trial.[23] A Cochrane review found that computer based interactive interventions for weight loss were associated with a mean weight loss of 1.5kg (95% CI 0.9 to 2.1kg) compared with no or minimal

intervention, an effect which is also consistent with our findings.[25] Systematic reviews on internet based telehealth interventions for smoking cessation show mixed effects, although mobile phone interventions based interventions are effective and telephone 'quitlines' can improve cessation rates in those people who pro-actively contact them.[24 46 47] It is important to note that the above reviews were all based on individuals who had the risk factor of interest and many trials only included individuals who were motivated to change the specific risk factor. In the Healthlines CVD risk trial only a proportion of participants had raised BP, obesity or were smokers at baseline, and they were not necessarily motivated to change the main factor contributing to their risk, so effects are likely to be smaller than in studies on specific risk factors.

The Healthlines intervention tested in this trial had a similar impact on reducing BP as the earlier trials by Bosworth *et al* which used a similar behavioural management system (but provided by nurses rather than lay staff and without incorporating the use of internet resources).[28 29] However, it had less impact than two trials from the USA which involved BP self-management with pharmacist management of medication by phone or over the internet.[41 42] The involvement of pharmacists to directly alter medication without the intermediate step of sending advice to primary care physicians may be associated with more effective optimisation of treatment, but could be problematic in a routine primary care context when patients often have comorbidities and other factors need to be considered in treatment decisions.

Two systematic reviews of telehealth interventions to reduce overall cardiovascular risk have recently been published.[14 48] Several studies demonstrated small improvements in BP and weight, findings with regard to cholesterol were equivocal, and there was no evidence of increased rates of smoking cessation. Our results are consistent with these findings but provide much stronger evidence from a large, rigorous and pragmatic trial.

Implications for clinicians and for policy

The development of the Healthlines Service reflected a conceptual framework which was based on promoting self-management, improving medication adherence and optimisation of drug treatment, improving co-ordination of care and the active engagement of patients and primary care clinicians.[18] This randomised controlled trial shows modest but cost effective benefit in cardiovascular risk reduction. Delineating how components of a multi-faceted intervention work, alone or in combination; their effect on physician practice in terms of optimisation/intensification of medicines and their effect on behaviour modification by patients is complex. What is clear is that patients who engaged with the intervention appear to gain the most in terms of cardiovascular risk but some components of the intervention, particularly optimisation/intensification of drugs, were ineffective. In order to improve the effectiveness of the intervention it will be important to target it at those

who are motivated to change their risk behaviours, and to improve communication with primary care prescribers with regard to drug treatment recommendations.

There has been considerable optimism about the potential of telehealth approaches to improve the accessibility, convenience and efficiency of health care. This study adds to the growing evidence base which suggests that healthcare delivery systems based on telehealth may be associated with some benefits but these should not be assumed. However, this study has demonstrated the feasibility of delivering an intervention on a wide scale at relatively low cost, and using non-clinically trained health advisors supported by computerised algorithms. This increases the capacity of the health care system to provide an intervention to large numbers of people. Further development of this type of intervention is justified to increase the effectiveness of the Healthlines approach.

Contributors

CS, AO'C, SH, JN, SL, LY, TF, AR, CP and AAM developed the protocol for the study, obtained funding, provided methodological advice and supervised the conduct of the trial. CS led protocol development and the funding application, acted as chief investigator with overall responsibility for the conduct of the trial, and led the drafting of the article. AO'C supervised the conduct of the trial in Sheffield. CT, MSM and LE acted as trial managers, co-ordinating the conduct of the trial across the centres. LE, AF, KG, and KH undertook participant recruitment and follow-up, data collection and data entry. DG developed the statistical analysis plan and undertook the statistical analysis. PD undertook the economic analysis. SL co-ordinated development and delivery of the intervention with NHS Direct. AAM supervised the statistical analysis. All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version of this manuscript. CS is guarantor.

Declaration of interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: support from NIHR in grant funding but no other support for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and no non-financial interests that may be relevant to the submitted work. The Healthlines patient portal is the intellectual property of Solent NHS Trust. The telephone algorithms were adapted with permission from a patient assessment system which is the

intellectual property of Duke University. Interested readers should refer to the website http://www.bristol.ac.uk/healthlines/ and contact the author for further information.

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The funder had no role in the conduct of the study, the writing of the manuscript or the decision to submit it for publication. The corresponding author (CS) had full access to all the data in the study and had final responsibility for the decision to submit for publication. CS, AOC and JN act as members of boards for NIHR but were not on the board which commissioned this project.

Ethical approval

The study was approved by the National Research Ethics Service Committee South West–Frenchay (Reference 12/SW/0009). All participants provided informed consent to take part in the trial.

Transparency

CS as guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained.

Data sharing

The research team will consider reasonable requests for sharing of patient level data. Requests should be made to CS. Consent for data sharing was not obtained but the presented data are anonymised and risk of identification is low.

Licence

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Figure 1. Flow of participants through trial comparing Healthlines cardiovascular disease intervention and usual care

(See PDF file Figure 1)

Box 1. Components of the Healthlines CVD risk intervention, reflecting the TECH conceptual mode.

Examples of strategies are show in italics

- Computerised behaviour management program
  - *Providing interactive scripts used by health advisors*
  - *Identifying patient goals and tailoring intervention.*
  - *Modules include:*
    - *Knowledge about cardiovascular risk and healthy lifestyles*
    - *Medication and side effects review*
    - *Blood pressure medication optimisation*
    - *Home BP monitoring*
    - *Statin medication review*
    - *Support for medication adherence*
    - *Smoking and nicotine replacement therapy*
    - *Healthy eating*
    - *Weight loss and Orlistat*
    - *Alcohol use*
    - *Exercise*
- Motivational interviewing
  - *Health advisors all trained in motivational interviewing*
- Self-monitoring and feedback
  - *BP online self-monitoring programme with automated feedback*
- Treatment optimisation and intensification
  - *Health advisors monitor treatment response. In patients with inadequate control, recent readings and a request to intensify treatment, along with reminders of treatment guidelines emailed to clinicians and copied to patients*
- Addressing medication adherence
  - *Monthly review of medication adherence; algorithmic scripts based on evidence based strategies to promote adherence*
- Improving care co-ordination
  - *sharing all information sent to clinicians with patients*
- Supporting primary care
  - *all aspects of the intervention designed to support rather than duplicate primary care*
- Strategies to promote patient engagement
  - *through continuity of care with the same advisor; providing technical support with getting online*
- Strategies to promote primary care clinician engagement
  - *emphasising evidence based nature of intervention components and how it can support their work in primary care*

Table 1 Baseline characteristics of participants allocated to usual care or the Healthlines intervention. Figures are numbers (percentages) unless otherwise stated.

	Usual care (n = 316)		Intervention (n = 325)	
Demographic data		**n/N**		**n/N**
Mean age at cardiovascular assessment (SD)	67.3 (4.7)	316	67.5 (4.9)	325
Number female (%)	21%	66/316	18%	60/325
Number White (%)	99%	313/316	99%	321/325
Current employment situation				
Number in full-time employment (%)	13%	39/311	17%	54/316
Number in part-time employment (%)	14%	43/311	9%	29/316
Number unemployed (%)	1%	4/311	1%	2/316
Number unable to work due to long-term illness/disability (%)	2%	7/311	1%	3/316
Number unable to work due to carer responsibilities (%)	1%	3/311	1%	2/316
Number fully retired from work (%)	63%	196/311	66%	210/316
Number looking after the home (%)	1%	3/311	1%	4/316
Number doing something else (%)	5%	16/311	4%	12/316
Occupation (most recent or current)				
Number in administrative or secretarial occupations (%)	11%	31/294	10%	29/294
Number in associate professional or technical occupations (%)	15%	45/294	12%	35/294
Number in elementary occupations (%)	10%	28/294	5%	16/294
Number of managers or senior officials (%)	19%	55/294	22%	65/294
Number in personal services (%)	2%	5/294	3%	9/294
Number of process, plant and machine operatives (%)	5%	15/294	6%	17/294
Number of professionals (%)	19%	57/294	22%	64/294
Number in sales and customer services (%)	4%	11/294	4%	13/294
Number in skilled trades (%)	16%	47/294	16%	46/294
Highest education qualification achieved				
Number with degree or higher degree (%)	21%	65/307	23%	72/318
Number with A levels or equivalent (%)	19%	58/307	17%	53/318
Number with GCSEs/O levels or equivalent (%)	45%	137/307	43%	136/318
Number with no qualifications (%)	15%	47/307	18%	57/318

	Usual care (n = 316)		Intervention (n = 325)	
Accommodation				
Own accommodation or buying with mortgage (%)	84%	264/315	87%	281/323
Part-rent or rent accommodation (%)	15%	46/315	12%	40/323
Live rent free (%)	2%	5/315	1%	2/323
Mean Index of Multiple Deprivation (SD)	16.7 (12.6)	316	15.5 (11.3)	325
Clinical data				
Mean QRISK2 score (SD)	30.8 (9.5)	316	31.1 (10.2)	325
Mean systolic blood pressure (SD)	148.1 (17.6)	316	147.6 (16.2)	325
Mean diastolic blood pressure (SD)	80.0 (10.4)	316	81.2 (9.6)	325
Mean weight (SD)	91.9 (18.9)	316	93.2 (17.3)	325
Mean body mass index (SD)	30.9 (5.7)	316	31.2 (5.4)	325
Mean total cholesterol (SD)	4.9 (1.2)	315	4.9 (1.2)	324
Mean total cholesterol/HDL ratio (SD)	4.2 (1.4)	315	4.2 (1.5)	323
Number of non-smokers (%)	33%	103/316	35%	114/325
Number of ex-smokers (%)	47%	148/316	50%	163/325
Number of light smokers (%)	9%	30/316	8%	25/325
Number of moderate smokers (%)	5%	17/316	5%	16/325
Number of heavy smokers (%)	6%	18/316	2%	7/325
Number taking anti-hypertensives (%)	61%	193/316	64%	209/325
Number taking lipid-lowering medication (%)	49%	153/312	49%	158/322
Number with diabetes (%)	20%	62/316	24%	77/325
Number with chronic kidney disease (%)	11%	34/316	6%	20/325
Number with atrial fibrillation (%)	6%	20/316	7%	23/325
Number with rheumatoid arthritis (%)	3%	8/316	2%	6/325

SD = Standard deviation; CVD = cardiovascular disease; GCSE = General Certificate of Secondary Education; HDL = high density lipoprotein cholesterol.

Table 2 Improving or maintaining cardiovascular risk as a binary outcome

	Usual care **N = 291 (12 months); 296 (6 months); 316 for imputed data** **% (n/total)**	**Intervention** **N = 295 (12 months); 301 (6 months); 325 for imputed data** **% (n/total)**	**Adjusted odds ratio (95% confidence interval)**	***P*-value**
Primary analysis				
Improved/maintained QRISK2 after 12 months	43% (124/291)	50% (148/295)	1.3 (1.0 to 1.9)	0.079
Secondary analysis				
Improved/maintained QRISK2 after 6 months	46% (137/296)	48% (145/301)	1.1 (0.8 to 1.5)	0.654
Sensitivity analyses of improved/maintained QRISK2 after 12 months				
Assuming all participants were one year older	45% (130/291)	52% (153/295)	1.3 (1.0 to 1.9)	0.096
Simple imputation, assuming missing binary outcome is non-response	40% (124/316)	46% (148/325)	1.3 (0.9 to 1.8)	0.109
Multiple imputation	44% (139/316)	50% (163/325)	1.3 (0.9 to 1.8)	0.115
Not including GP practice as a random effect	43% (124/291)	50% (148/295)	1.3 (1.0 to 1.9)	0.079
Adjusted by days since randomisation to primary outcome assessment	43% (124/291)	50% (148/295)	1.3 (1.0 to 1.9)	0.094

All analyses are adjusted by site (Bristol, Sheffield or Southampton) and baseline QRISK2 score. GP practice is included as a random effect unless otherwise specified. Analyses are further adjusted by other covariates if specified.

Table 3 Sub-group analyses of primary outcome

	Improving or maintaining QRISK2 at 12-month follow-up		Adjusted odds ratio[a] (95% confidence interval)	Interaction *P*-value
	Usual care N = 291	Intervention N = 295		
Baseline CVD assessment age group				
40-59	54% (7/13)	61% (11/18)	1.5 (0.3 to 6.6)	
60-69	44% (78/177)	49% (75/152)	1.2 (0.8 to 1.9)	
≥70	39% (39/101)	50% (62/125)	1.6 (0.9 to 2.8)	0.708
Sex				
Male	46% (105/227)	51% (125/243)	1.2 (0.9 to 1.8)	
Female	30% (19/64)	44% (23/52)	1.8 (0.8 to 4.0)	0.369
Baseline QRISK2 score				
17.3-24.9	37% (37/101)	45% (44/98)	1.4 (0.8 to 2.5)	
25.0-29.9	38% (26/68)	44% (35/79)	1.2 (0.6 to 2.4)	
≥30.0	50% (61/122)	58% (69/118)	1.4 (0.8 to 2.4)	0.947
Baseline modifiable risk factor				
Systolic blood pressure <140	33% (30/90)	41% (35/85)	1.5 (0.8 to 2.8)	
Systolic blood pressure ≥140	47% (94/201)	54% (113/210)	1.3 (0.9 to 1.9)	0.726
Body mass index <30.0	50% (65/131)	52% (67/129)	1.1 (0.6 to 1.8)	
Body mass index ≥30.0	37% (59/160)	49% (81/166)	1.7 (1.1 to 2.6)	0.200
Current smoker	51% (29/57)	53% (23/43)	1.1 (0.5 to 2.5)	
Not current smoker	41% (95/234)	50% (125/252)	1.4 (1.0 to 2.1)	0.546

a Odds ratio comparing intervention versus usual care.

All analyses are adjusted by site (Bristol, Sheffield or Southampton), baseline outcome and baseline QRISK2 score. GP practice is included as a random effect.

Table 4 Secondary outcomes: QRISK2 score as a continuous outcome and individual modifiable cardiovascular risk factors of blood pressure, cholesterol, weight and body mass index.

	Usual care N = 296 (6 months); 291 (12 months)		Intervention N = 301 (6 months); 295 (12 months)			
	Unadjusted mean (SD)	**N**	**Unadjusted mean (SD)**	**N**	**Adjusted difference in means (95% confidence interval)**	***P*-value**
QRISK2 score as continuous variable						
6 months	31.0 (9.5)	296	31.4 (10.3)	301	0.1 (-0.2 to 0.4)	0.489
12 months	31.2 (10.3)	291	31.3 (10.7)	295	-0.4 (-1.2 to 0.3)	0.269
Systolic blood pressure (mmHg)						
6 months	141.4 (15.4)	296	141.0 (15.1)	301	0.0 (-1.9 to 1.9)	0.997
12 months	142.2 (16.1)	291	139.6 (14.0)	295	-2.7 (-4.7 to -0.6)	0.011
Diastolic blood pressure (mmHg)						
6 months	78.0 (9.7)	296	78.2 (9.9)	301	-0.6 (-1.8 to 0.6)	0.337
12 months	78.7 (9.9)	291	76.6 (9.2)	295	-2.8 (-4.0 to -1.6)	<0.001
Total cholesterol (mmol/L)[a]						
12 months	4.7 (1.1)	288	4.6 (1.2)	295	-0.1 (-0.2 to 0.0)	0.167
Total cholesterol/HDL ratio [a]						
12 months	4.0 (1.5)	287	4.0 (1.7)	294	-0.1 (-0.2 to 0.1)	0.451
Weight (kg)						
6 months	91.1 (18.4)	296	91.7 (17.7)	301	-0.9 (-1.5 to -0.2)	0.006
12 months	91.2 (19.1)	291	91.3 (17.5)	293	-1.0 (-1.8 to -0.3)	0.008
Body mass index (kg/m^2)						
6 months	30.6 (5.4)	296	30.7 (5.5)	301	-0.3 (-0.5 to -0.1)	0.006
12 months	30.8 (5.7)	291	30.5 (5.4)	293	-0.4 (-0.6 to -0.1)	0.008

[a] Cholesterol was not re-measured after 6 months. The baseline cholesterol measurement was used to calculate QRISK2 at 6 months.

HDL = high density lipoprotein.

All analyses are adjusted by site (Bristol, Sheffield or Southampton), baseline QRISK2 score and baseline outcome. GP practice is included as a random effect.

Table 5 Secondary outcome: smoking

	Usual care **N = 296 (6 months); 291 (12 months)** **% (n)**	**Intervention** **N = 301 (6 months); 295 (12 months)** **% (n)**	**Adjusted odds ratio (95% confidence interval)**	***P*-value**
Smoker at 6 months:				
Yes	18% (52/296)	15% (45/301)	N/A	N/A
No	82% (244/296)	85% (256/301)	0.3 (0.1 to 1.2)	0.099
Smoker at 12 months:				
Yes	18% (52/291)	17% (49/295)	N/A	N/A
No	82% (239/291)	83% (246/295)	0.4 (0.2 to 1.0)	0.061

All analyses are adjusted by site (Bristol, Sheffield or Southampton), baseline QRISK2 score and by baseline smoking category (non-smoker, ex-smoker, light smoker, moderate smoker, heavy smoker). GP practice is included as a random effect.

Table 6 Secondary outcomes at 12 months follow-up

	Usual care N = 300		Intervention N = 300			
	Unadjusted mean (SD)	**N**	**Unadjusted mean (SD)**	**N**	**Adjusted difference in means (95% confidence interval)**	***P*-value**
Quality of life (EQ-5D-5L)[32]	0.78 (0.2)	297	0.81 (0.2)	295	0.01 (-0.01 to 0.03)	0.410
Patient behaviours						
Exercise behaviour (heiQ subscale 'Health directed behaviour')[a33]	2.9 (0.8)	294	3.0 (0.8)	297	0.1 (0.0 to 0.2)	0.003
Diet (Starting the Conversation questionnaire)[a34]	10.3 (2.1)	299	10.9 (2.1)	300	0.6 (0.4 to 0.9)	<0.001
Patient experience						
Satisfaction with treatment[a,b]	3.7 (0.8)	215	3.9 (0.7)	244	0.1 (0.0 to 0.3)	0.032
Satisfaction with amount of support received[a,b]	2.8 (0.6)	207	3.1 (0.5)	260	0.3 (0.2 to 0.4)	<0.001
Patient perceived access to care[a,b]	5.5 (1.7)	293	5.8 (1.3)	287	0.3 (0.0 to 0.5)	0.015
Self-management skills and self- efficacy (heiQ)[33]						
Self-monitoring and insight[a]	3.2 (0.4)	295	3.3 (0.4)	295	0.1 (0.0 to 0.1)	0.073
Constructive attitudes and approaches[a]	3.3 (0.5)	296	3.4 (0.5)	295	0.0 (0.0 to 0.1)	0.628
Skill and technique acquisition[a]	3.1 (0.5)	297	3.2 (0.5)	295	0.1 (0.1 to 0.2)	<0.001
Health services navigation[a]	3.1 (0.6)	296	3.2 (0.5)	297	0.0 (0.0 to 0.1)	0.268
Medication adherence (Morisky)[35 a]						
Anti-hypertensives[c]	3.8 (0.5)	194	3.9 (0.3)	203	0.1 (0.0 to 0.2)	0.013
Statins[c]	3.6 (0.8)	165	3.8 (0.5)	169	0.2 (0.1 to 0.3)	0.005
Health literacy (eHEALs)[36 a]	3.9 (0.7)	296	4.0 (0.7)	295	0.1 (0.0 to 0.2)	0.128
Care coordination (Haggerty)[37]						
Role clarity and co-ordination[a]	2.9 (0.5)	247	3.0 (0.3)	263	0.1 (0.0 to 0.1)	0.015
Evidence of a care plan[a]	3.8 (2.1)	209	4.9 (2.0)	236	1.2 (0.8 to 1.5)	<0.001
Overall experience of organisation of healthcare[a]	3.6 (0.9)	296	3.8 (0.7)	296	0.1 (0.0 to 0.2)	0.044

Self-organisation of healthcare [a]	3.9 (1.1)	283	3.8 (1.0)	287	-0.1 (-0.2 to 0.1)	0.368
Use of telehealth [a,b,c]						
Online searching	1.6 (0.7)	297	1.6 (0.7)	296	0.1 (-0.0 to 0.2)	0.097
Online forum or group	1.1 (0.3)	295	1.1 (0.4)	298	0.0 (-0.0 to 0.1)	0.289

All analyses are adjusted by site (Bristol, Sheffield or Southampton), baseline outcome (if measured) and baseline QRISK2 score. GP practice is included as a random effect.

a Higher score is more positive (less access difficulties, greater satisfaction)

b Based on scales generated prior to the main trial analysis using principal components analysis and incorporating questions taken from existing validated questionnaires or constructed for this research.

[c] Only applicable to those taking anti-hypertensives or statins respectively

d 5 level ordered categorical variable (Never/almost never to Daily /almost daily)

Table 7 Complier-average causal effect analysis of the primary outcome

	Maintenance/reduction in QRISK2 at 12-month follow-up		Partial compliers classified as non-compliers	Partial compliers classified as full compliers
			Intervention vs. Usual Care	Intervention vs. Usual Care
	Usual care N=291	Intervention N=293	Unadjusted odds ratio (95% CI)	Unadjusted odds ratio (95% CI)
Amount of intervention received:				
None (0-2 encounters)	43% (124/291)	29% (4/14)		
Partial (3-11 encounters)		44% (77/177)		
Full (12-13 encounters)		65% (66/102)	2.4 (1.4 to 4.3)	1.4 (1.0 to 1.9)

Three participants who never received the Healthlines intervention and two participants who only received unscheduled non-encounter calls are categorised as receiving none of the intervention. Two intervention arm participants have missing encounter data.

Table 8 Treatment optimisation: cardiovascular risk-related medication prescriptions over the trial

	Usual care N = 316		Intervention N = 325		Intervention vs. Usual care	
	%	Participants (n)	%	Participants (n)	Adjusted odds ratio (95% CI)	*P*-value
Experienced at least one change in medication over 12 month period (medical records data)						
Antihypertensive	32%	100/316	38%	123/325	1.3[a] (0.9 to 1.8)	0.117
Cholesterol drugs including statins	22%	71/316	26%	84/325	1.2[a] (0.8 to 1.7)	0.327
Self-reported use of medication over 12 month period (questionnaire data)						
Antihypertensive	68%	196/289	70%	202/287		
Statin	57%	165/297	57%	166/290		
Prescribed at least one medication over trial period (medical records data)						
Antiplatelet	18%	57/316	19%	62/325		
Cholesterol drugs including statins	61%	192/316	62%	201/325		
Smoking cessation	1%	3/316	2%	5/325		
Obesity medication	1%	2/316	1%	4/325		
Antihypertensive	70%	222/316	73%	236/325		
Prescribed antihypertensive drug by drug class over trial period (medical records data)						
ACE inhibitors or ARBs	50%	159/316	52%	170/325		
Beta blockers	18%	58/316	16%	52/325		
Calcium blockers	36%	114/316	40%	129/325		
Diuretics	29%	90/316	29%	93/325		
Other	8%	26/316	8%	26/325		

ACE inhibitors = Angiotensin-converting-enzyme inhibitor, ARBs = Angiotensin receptor blockers.

[a] Only these between treatment-group comparisons are analysed because treatment optimisation was a key aspect of the intervention. Analyses are adjusted by site (Bristol, Sheffield or Southampton) and baseline QRISK2 score. GP practice is included as a random effect.